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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/943,075	08/30/2001	Steven N. Popoff	71369.262 and PFI-015	7695

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EXAMINER

PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
1632	

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16

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 09/943,075	Applicant(s) Popoff et al.
	Examiner Scott D. Priebe, Ph.D.	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1)  Responsive to communication(s) filed on Jan 29, 2003
- 2a)  This action is FINAL.                    2b)  This action is non-final.
- 3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

- 4)  Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above, claim(s) 6-8, 11-13, 17-19, 21-26, 28, 32-38, and 43-46 is/are withdrawn from consideration.
- 5)  Claim(s) 9, 14, 40, and 41 is/are allowed.
- 6)  Claim(s) 1-5, 10, 15, 16, 20, 27, 30, 31, 39, and 42 is/are rejected.
- 7)  Claim(s) 29 is/are objected to.
- 8)  Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9)  The specification is objected to by the Examiner.
- 10)  The drawing(s) filed on February 29, 2002 is/are a)  accepted or b)  objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12)  The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13)  Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)  All b)  Some\* c)  None of:

1.  Certified copies of the priority documents have been received.
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)  The translation of the foreign language provisional application has been received.

- 15)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). <u>2</u>	6) <input type="checkbox"/> Other: _____

Art Unit: 1632

### **DETAILED ACTION**

The amendments filed 1/29/02 and 2/12/02 have been entered. Claims 10, 14, 15, 25, 29, and 32 have been amended. Claims 39-46 have been added.

#### *Election/Restriction*

Applicant's election with traverse of Group I, claims 1-5, 9, 10, 14-16, 20, 27, 29-31, and 39-42 in Paper No. 14 filed 1/29/03 is acknowledged. The traversal is on the ground(s) that all groups relate to osteoactivin and therefore one invention and that search and examination could be made without serious burden. This is not found persuasive because Applicant has provided no reasons to support the assertions, or to identify any error in the restriction requirement. The different classification of the various inventions is evidence that in fact a serious burden would be imposed by search and examination of all claimed inventions. As shown by the rejections over the prior art set forth below, osteoactivin, while under different names, e.g. nbm, was known in the prior art and does not provide a link for a single general inventive concept.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6-8, 11-13, 17-19, 21-26, 28, 32-38, and 43-46, in their entirety, and claims 20, 27, and 29-31, in part as directed to an agent other than nucleic acid, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14.

Art Unit: 1632

***Claim Objections***

Claims 20, 27, and 29-31 are objected to because of the following informalities: these claims are directed to non-elected inventions, there being no allowable generic or linking claim. Appropriate correction is required.

Claim 29 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must depend from multiple claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claim 29 not been further treated on the merits.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims are directed to “a nucleic acid molecule”. The claims recite limitations on the structure, but not the form of the nucleic acid molecule, e.g. isolated. Consequently, the claims read on endogenous genomic DNA and mRNA present in a living Norway rat, and do not distinguish the claimed nucleic acid from those found in nature. This rejection would be overcome by amending the claims to indicate the hand of man, e.g. by claiming “isolated” nucleic acid molecules.

Art Unit: 1632

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 4, 10, 15, 39 and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule encoding SEQ ID NO: 2 (claims 3, 10, 15) or SEQ ID NO: 2 (claims 4, 39, 42), does not reasonably provide enablement for nucleic acid molecules encoding any other polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make use the invention commensurate in scope with these claims.

Claims 16, 20, 27, 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a nucleic acid molecule that encodes an active osteoactivin protein and methods and compositions of the nucleic acid molecule for its use in producing osteoactivin in culture or in stimulating bone formation in a mammal. The claims are broadly directed to a nucleic acid which encodes osteoactivin. Claims 3 and 4 limit the nucleic acid molecules to those which hybridize under moderately stringent conditions to or are at least 92% identical with the open reading frame of SEQ ID NO: 1, nucleotides 115-1830, encoding SEQ ID

Art Unit: 1632

NO: 2. Claim 3 would embrace the disclosed human and mouse homologs of the rat sequence (SEQ ID NO: 1), whereas claim 4 would exclude the mouse and human sequences. While the claims read on naturally occurring sequences, they read primarily on non-natural sequences which would encode a protein with osteoactivin function or activity, which would require one of skill in the art to make such sequences *de novo*.

The specification provides a comparison between the rat, mouse and human sequences, and presents an analysis of the rat protein for secretion peptides, glycosylation sites, possible transmembrane spanning regions, etc. However, the specification fails to disclose any assay for the detection of osteoactivin activity, whether biochemical or physiological, and thus fails to provide the means by which nucleic acid molecules which either hybridize to or are at least 92% identical to SEQ ID NO: 1 but encode inactive polypeptides can be distinguished from those readable on the claims, which do encode a polypeptide with osteoactivin activity. In addition, the specification does not provide any information on what amino acid residues are necessary and sufficient for the undisclosed osteoactivin activity. The specification also provides no teachings on what amino acid sequence modifications, e.g. insertions, deletions and substitutions, would be permissible in a variant polypeptide that would improve or at least would not interfere with the biological activity or structural features necessary for the biological activity and stability of the protein. Furthermore, it is known in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its

Art Unit: 1632

tertiary structure is neither well understood nor predictable (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976) discloses that even for peptide hormones, which are much smaller than the instant osteoactivin protein, one cannot predict variant amino acid sequences for a biologically active polypeptide. Rather one must engage in “case to case painstaking experimental study” to determine active variants (see page 7). Consequently, excessive trial and error experimentation would have been required to identify the necessary nucleic acid sequence derivatives encoding a protein with osteoactivin activity with an amino acid sequence differing from SEQ ID NO: 2 since the amino acid sequence of such polypeptides could not be predicted - even were the activity known.

As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

In *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with

Art Unit: 1632

a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 USC 112, 1st para., if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. This is the case here, where specification discloses only one putative functional amino acid sequences, SEQ ID NO: 2, for a polypeptide having the necessary activity, and provides no guidance on determining which polypeptide variants of SEQ ID NO: 2 would have osteoactivin activity.

To put the situation in perspective, the number of possible amino acid sequences of 570 amino acids in length is  $20^{572}$  (approx.  $10^{744}$ ). The number of possible nucleotide or amino acid sequences that are of a given %identity relative to a reference sequence, where all differences between the possible sequences and the reference sequence are substitutions, can be calculated by the following expansion formula:

$$N = XL + X^2L(L-1)/2! + X^3L(L-1)(L-2)/3! + \dots + X^{n-1}L(L-1)(L-2)\dots(L-(n-2))/(n-1)! + X^nL(L-1)(L-2)\dots(L-(n-1))/n!$$

where N is the number of possible sequences, X is the number of different residues that can be substituted for a residue in the reference sequence, L is the length of the reference sequence, n is the maximum number of residues that can be substituted relative to the reference sequence at a given % identity. For a nucleotide sequence, X is 3 (alternate nucleotides); for an amino acid sequence, X is 19 (alternate amino acids). The  $n^{\text{th}}$  term of the expansion can be rewritten as:

Art Unit: 1632

$$x^n \cdot \frac{L!}{(L-n)!n!}$$

For a 572 amino acid sequence that is at least 92% identical to a reference sequence of 572 amino acids, e.g. SEQ ID NO: 2, the number of possible sequences having 44 amino acid substitutions relative to the reference (the penultimate term of the formula) is approximately  $3 \times 10^{122}$ , whereas the number of possible sequences having 45 amino acid substitutions relative to the reference (the final term of the formula) is approximately  $1.6 \times 10^{179}$ . So the last term is approximately equal to N, i.e. the preceding terms contribute little to the total. Also, as the number of permitted substitutions increases the number of possible variant sequences increases geometrically. In a genus of polypeptides that are at least 92% identical to a reference, nearly all will be exactly 92% identical. While limiting the scope of potential sequences to those that are at least 92% identical to a reference greatly reduces the number of potential sequences to test, it does not do so in any meaningful way. The mass of the Earth is about  $6 \times 10^{24}$  kg. One microgram of 1716 nucleotide dsDNA molecules (required to encode 572 amino acids) contains approximately  $5 \times 10^{11}$  DNA molecules. If it were possible to convert the mass of the Earth ( $6 \times 10^{30}$  µg) into such DNA molecules, one would obtain about  $3 \times 10^{41}$  DNA molecules. Thus, one would require about  $5 \times 10^{137}$  times the mass of the Earth of DNA to produce just one nucleic acid molecule encoding each of the  $10^{179}$  possible amino acid sequences differing from SEQ ID NO: 2 by substitution of 8% of their amino acids.

Art Unit: 1632

Therefore, inclusion of the recited structural relationships in the claims do not distinguish the instant fact situation from those reviewed in *Amgen*. Thus, even were an assayable activity of osteoactivin disclosed, the instant specification would be inadequate to describe and enable how to make the nucleic acid molecules as broadly as they are claimed here.

Claims 16, 20, 27, 30, and 31 are directed to therapeutic compositions comprising nucleic acid molecules encoding osteoactivin and methods of using such compositions to stimulate bone formation in a mammal, such as in the treatment of bone disorders. The instant specification presents the problem (page 2) that pharmaceutical approaches to managing osteoporosis are of limited effectiveness, and that alternative therapies are needed to treat bone disorders. The claimed method is advanced as a therapy to meet that need. However, the specification presents no evidence that would lead one of skill in the art to believe that expression of exogenous osteoactivin from a gene therapy vector would stimulate bone growth. The specification presents no experiments where such a hypothesis was tested, much less supported, using either cells in culture or animals. While the specification presents evidence that the osteoactivin protein is involved somehow in bone formation or in osteoblast function, that is the full extent of the conclusions which may be reasonably drawn. In summary, the specification shows that osteoactivin is expressed in osteoblasts in normal rats and overexpressed in osteopetrotic rats, that osteoactivin is secreted and may be a membrane protein, and that antibodies against osteoactivin inhibit calcium deposition by cultured osteoblasts. The specification suggests that the inhibition of calcium deposition indicates that the antibodies inhibit osteoblast differentiation.

Art Unit: 1632

While that may be true, the assay presented does not test this directly. Since calcium deposition is a function of mature osteoblasts, these results may also be explained as an inhibition of that mature osteoblast function, rather than inhibiting osteoblast maturation. Also, evidence that osteoactivin may be necessary for osteoblast function does not indicate that it is sufficient for promoting such function when in excess.

The actual function of osteoactivin in osteoblasts or in bone was (and still is) unknown. It does not necessarily follow from the results presented in the specification that providing exogenous nucleic acid encoding osteoactivin would stimulate bone formation, as required by the claimed invention. Weterman et al. (Int. J. Cancer 60 (1): 73-81, 1995) isolated cDNA of the human nmb gene, the human osteoactivin, from lowly metastatic human melanoma cells. Transfection of a partial cDNA (lacks coding sequence for the signal peptide) into highly metastatic melanoma cells lead to slower subcutaneous growth of implanted cells and a reduction in metastatic potential. Anderson et al. (Nature Genetics 30: 81-85, Jan. 2002) discloses that DBA/2J mice develop pigmentary glaucoma as a result of a loss of function mutation in the mouse nmb gene (murine osteoactivin gene). No other phenotype of these mice is reported, such as osteopenia. If, as Applicant proposes, osteoactivin stimulates osteoblast proliferation and/or differentiation, one might expect a mouse deficient in osteoactivin to display some phenotype consistent with that hypothesis, such as osteopenia. Sanicola-Nadel et al. (WO 97/44460) disclose that rat osteoactivin (which they call a kidney injury-related protein) is overexpressed in ischemic, normal rat kidney, apparently in infiltrating cells. Taken together, these results suggest

Art Unit: 1632

a more fundamental or basic function for osteoactivin than in promotion of osteoblast function and bone deposition. While these results do not necessarily preclude Applicant's hypothesis, they certainly fail to support it. Consequently, the prior art (and post-filing art) fail to support the hypothesis, and when combined with the lack of any disclosed direct experimental test of Applicant's hypothesis, one of skill in the art would have no basis to reasonably conclude that the claimed invention would succeed. There is no evidence that the specification offers a solution to the problem set forth in the specification of providing alternative therapies are to treat bone disorders. Though not controlling, the lack of working examples, is, nevertheless, a factor to be considered in a case involving both physiological activity and an undeveloped art. When a patent applicant chooses to forego exemplification and bases utility on broad terminology and general allegations, he runs the risk that unless one with ordinary skill in the art would accept the allegations as obviously valid and correct, the PTO may, properly, ask for evidence to substantiate them. *Ex parte Sudilovsky*, 21 USPQ2d 1702, 1705 (BPAI 1991); *In re Novak*, 134 USPA 335 (CCPA 1962); *In re Fouche*, 169 USPQ 429 (CCPA 1971).

The general subject area of the claimed invention is *in vivo* gene therapy, which at the time the invention was made was highly unpredictable and still largely undeveloped art, despite high skill in the art and extensive experimentation. Orkin et al. reviews the infant state of the art of gene therapy before the instant invention was made. The overall conclusions were: 1) gene therapy for each disease would present its own scientific and clinical challenges; 2) no successful gene therapy protocol was known; 3) significant problems remained in all aspects of gene

Art Unit: 1632

therapy, especially with respect to effective expression vectors; 4) the pathophysiology of diseases to be treated were poorly understood; 5) one cannot predictably extrapolate the result of one animal model, such as mouse, to treatment of a disease in a different animal, such as human; 6) assessment of known gene therapy protocols was hindered by poor gene transfer, reliance on qualitative, rather than quantitative assessments of gene transfer, lack of suitable controls and poor definition of biochemical or disease endpoints; and 7) that gene therapy has been oversold, and the impression that gene therapy is successful is mistaken (pages 1-2). Each of the defects in the gene therapy art as a whole cited by Orkin et al. applies to the instant invention. Verma et al. (Nature 389: 239-242, 1997) reiterates the finding in Orkin that not a single successful gene therapy protocol has been described in the art and that lack of efficient gene delivery and sustained expression remained the Achilles heel of gene therapy (see page 239). The instant specification does not correct the deficiencies in the prior art regarding gene therapy. Rather, the specification relies solely upon the prior art for teaching gene therapy. The sole guidance in the specification is to administer the nucleic acid molecules, without teaching the appropriate target cells, how to deliver the nucleic acid to those target cells, or how to achieve sufficient levels of transfection and expression in order to obtain a therapeutically relevant response. Verma clearly discloses that serious problems existed in this art such that no unequivocal success had been obtained for the treatment of any disease. Verma reports optimism that the problems would be surmounted and that gene therapy would one day be routine, however, there is no evidence of record that it was routine at the time the invention was made, quite the contrary. Orkin clearly

Art Unit: 1632

makes the point that artisans in the field of gene therapy were overly optimistic and had oversold gene therapy. Rosenberg et al. (Science 287 : 1751, 2000) reported that at the time the instant application was filed, there was still no unequivocal instance of clinical efficacy with gene therapy, and that those in the field were still guilty of overselling gene therapy, despite a decade of failure.

It has long been recognized in the chemical and biological arts that the unpredictability of a particular art area may alone provide a reasonable doubt as to the accuracy of a broad statement made in support of the enablement of a claim. *Ex parte Singh*, 17 USPQ2d 1714, 1715 (BPAI 1991), *In re Marzocchi*, 169 USPQ 367, 369-370 (CCPA 1971). As set forth in *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Consequently, the lack of evidence from the specification and prior art that the invention would be successful, the lack of guidance on actually carrying out the claimed therapy, the high unpredictability of gene therapy, the inherent unpredictability of the physiological arts and of the success of an untried, untested method, the lack of any working example either of the claimed method or even of preliminary tests *in vitro* supporting the proposed effect of increasing

Art Unit: 1632

osteoactivin levels, it clearly would have required undue experimentation to practice the claimed invention.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in:
  - (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
  - (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-5 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Xu et al.

GenBank Acc. No. AF184983, 21 October 1999.

Xu discloses a nucleic acid molecule comprising nucleotides 115-1830 of instant SEQ ID NO: 1 and encoding instant SEQ ID NO: 2. The reference constitutes knowledge of the inventions by others in that the authorship includes individuals not named as inventors.

Art Unit: 1632

Claim 3 are rejected under 35 U.S.C. 102(a) as being anticipated by Bachner, GenBank Acc. No. AJ251685, 07 Jan. 2000.

Bachner discloses a nucleic acid molecule comprising a nucleotide sequence (nucleotides 91-1812) which is 91% identical to nucleotides 115-1830 of instant SEQ ID NO: 1, and encodes the murine glycoprotein nmb protein (now known as Gpnmb). This sequence is essentially identical to instant SEQ ID NO: 7, which the instant specification discloses as being the murine homologue of the rat osteoactivin. The extensive sequence identity between the murine and rat sequences would be expected to mediate hybridization under moderate stringency conditions and higher, e.g. there are several stretches of at least 50 nucleotides in common and one stretch of 89 nucleotides.

Claims 3, 10, 15, 16, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Sanicola-Nadel et al., WO 97/44460.

Sanicola-Nadel discloses a nucleic acid molecule, SEQ ID NO: 4, encoding a protein, SEQ ID NO: 5, isolated from ischemic kidney of a rat. Sanicola-Nadel discloses expression vectors and therapeutic compositions comprising the nucleic acid molecule and methods for producing the protein from cultured cells transfected with an expression vector. Nucleotides 107-1822 of SEQ ID NO: 4 differ from nucleotides 115-1830 of instant SEQ ID NO: 1 by 4 nucleotides, and SEQ ID NO: 5 differs from instant SEQ ID NO: 2 by 4 amino acids.

Art Unit: 1632

While Sanicola-Nadel does not teach that the protein of SEQ ID NO: 5 is osteoactivin, it is essentially identical to instant SEQ ID NO: 2, and presumably is an allelic form. To the extent that claim 20 includes nucleic acid encoding rat osteoactivin, the prior art expression vectors meet the limitation of agent. (pages 10, 25-29, 38-43, claims 1-7, Fig. 3)

Claims 3, 10, 15, 16, and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Strachan et al., US 6,242,419.

Strachan discloses a nucleic acid molecule, SEQ ID NO: 27, encoding a protein, SEQ ID NO: 36, isolated from lymph nodes of a fsn *-/-* mouse. Strachan discloses expression vectors and therapeutic compositions comprising the nucleic acid molecule and methods for producing the protein from cultured cells transfected with an expression vector. (col. 9, lines 20-34; col. 10, line 49 to col. 11, line 27; col. 53-56; col. 67-70.) SEQ ID NO: 27 of Strachan corresponds to instant SEQ ID NO: 7, the mouse nbm.

While Strachan does not teach that the protein of SEQ ID NO: 36 is osteoactivin, it is essentially identical to the murine osteoactivin/nbm protein disclosed in the instant specification. To the extent that claim 20 includes nucleic acid encoding murine osteoactivin, the prior art expression vectors meet the limitation of agent.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are

Art Unit: 1632

also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Scott D. Priebe, Ph.D.  
Primary Examiner  
Technology Center 1600  
Art Unit 1632